

Clinical trials for rare and ultra-rare diseases: summary for people living with rare conditions

A rare disease is defined as affecting fewer than 1 in 2,000 people. Collectively, rare diseases affect 1 in 17 people – over 3.5 million people in the UK – and yet few have available treatment options. However, running clinical trials to develop safe and effective new treatments can be a challenge for rare diseases. In March 2022, people living with rare conditions and those who care for them came together with organisations that run and regulate clinical trials to discuss ways to overcome some of these challenges in a [workshop](#) run by the Academy of Medical Sciences' FORUM and Faculty of Pharmaceutical Medicine.¹

This summary highlights elements of the workshop discussions thought to be important and relevant by some of the people living with rare conditions/carers who attended the workshop.

What is a clinical trial and why are they important?

Clinical trials test new treatments in multiple people to help decide whether the treatments are safe, have the desired effect on a disease, and are an improvement on the current standard treatment for that disease. Clinical trials also teach us important information about a specific drug (for example, the most effective dose that minimises any side effects) and/or the disease in question. To find out more about clinical trials, watch [this video](#), read this [article](#), or see the 'find out more' box at the end of this summary.

It is important that clinical trials produce enough relevant, high-quality evidence for medicines regulators to make this judgement and approve the treatment for use in patients. The low number of people living with a particular rare condition often makes it difficult to recruit enough people to take part in a clinical trial to gather this evidence.

People living with rare conditions and their carers/families who contributed to the workshop talked about some of the benefits of participating in clinical trials. They felt clinical trials enabled them to:

- Have access to a new treatment that might improve their quality of life
- Meet relevant researchers, healthcare practitioners and other people living with their condition
- Contribute to clinical research that will benefit the wider community living with the condition (even if the treatment did not work as expected)
- Take action, giving hope and motivation for the future, particularly where a condition has no existing treatment.

They also talked about challenges of participating in clinical trials for rare conditions, including:

- Difficulty finding out about relevant clinical trials
- Strict eligibility criteria
- The administrative, financial and logistical burden of participating in trials

¹ The Academy of Medical Sciences' [FORUM](#) provides an independent platform for senior leaders from across academia, industry, government, and the charity, healthcare and regulatory sectors to come together with patients and take forward national discussions on scientific opportunities, technology trends and associated strategic choices for healthcare and other life sciences sectors.

- The lack of communication between trial staff and those involved in the routine care of trial participants
- The mental and physical load of participation whilst managing their condition.

During the workshop, attendees discussed how to overcome and reduce some of these challenges.

Finding clinical trials to participate in

People living with a rare condition often do not know how to find out about relevant clinical trials once diagnosed. Because the conditions are rare, clinicians (and other healthcare professionals) are often unfamiliar with the condition and relevant ongoing clinical trials, and so less able to help.

The low numbers of people living with a particular rare condition means it is particularly important that all people eligible to take part in a clinical trial for a rare condition are aware of the options available to them. Suggestions of how you can find out about ongoing clinical trials are in the 'find out more' box at the end of this summary.

Most clinical trials have criteria people must meet to be allowed to participate. These are usually published online but clinical trial staff and some healthcare professionals will be able to give advice about whether a person is eligible.

To ensure the results of a clinical trial are valid and complete, it is important (where possible) for trial participants to be able to continue participating to the end of the trial. To help with this, clinical trial staff should work to make participation as manageable as possible and ensure potential participants carefully consider what is involved with the trial beforehand. Workshop attendees pointed out the importance of making information leaflets for potential participants easily understandable and accessible, including the language and format used.

Reducing the challenges of participating in a clinical trial

Participating in a clinical trial for a rare condition can come with specific challenges. Workshop attendees strongly felt that trial participants should be provided with more support to overcome these so that they can continue to participate in a trial.

Clinical trials for rare conditions can often involve more travel to reach trial centres than other kinds of clinical trial. This is because the organisation running the clinical trial needs to recruit people with rare conditions from a large area, often from many countries, to ensure there are enough trial participants. This travel can pose significant administrative, financial, and logistical challenges for people living with rare conditions and their families, affecting their quality of life and their ability to participate. Organisations such as the [Rare Diseases Research Partners](#) provide support for people, including by helping to organise their travel and accommodation.

Another way of reducing the amount of travel is to allow for trial participation from home or locally; for example, administering the treatment being investigated at home or using virtual communication methods such as video calls to monitor and assess trial participants. However, trial participants would need expert support and training, and care should be taken to avoid excluding people not able to use the technologies needed for home participation.

Usually, the healthcare professionals looking after a person's participation in a clinical trial are not the same as the healthcare professionals providing their routine care. A lack of communication between these groups, and also with the trial participant themselves, can lead to uncertainty and distress when dealing with potential side effects of the treatment being

tested. Communication is made more challenging because, often, neither the participant nor the trial staff they interact with know whether the participant is receiving an active drug or an inactive drug (placebo). Usually, this information is only revealed at the end of the trial, to avoid biasing the results. Workshop attendees suggested that a named member of trial staff be appointed as a main point of contact with trial participants and relevant healthcare professionals to answer questions, provide information, and help support trial participants.

Nothing about us without us – clinical trial design

Consulting with people living with rare conditions and their carers/families is essential when designing and conducting a clinical trial to ensure that the results will be relevant to them, and that the clinical assessments will be manageable for trial participants.

Workshop attendees also discussed novel clinical trial designs that could help make clinical trials for rare conditions more informative and more efficient. These included:

- 'Umbrella' trials, where multiple new treatments are tested in the same trial
- 'Basket' trials, where the efficacy of one new treatment is tested on multiple diseases
- 'Adaptive' clinical trials, which change in pre-defined ways in response to data as it is gathered – for example, stopping a clinical trial early if the treatment does not seem to be having the expected effect.

Clear communication of the advantages and disadvantages of novel clinical trial designs will be essential to make sure they are understood by and acceptable to people living with rare conditions and their families.

Find out about ongoing clinical trials for your condition

In addition to asking your doctor or healthcare professional, you can:²

- **Search for clinical trials online:** There are databases that collect ongoing clinical trials (such as ClinicalTrials.gov) but many of them are not written in easily understandable language or are difficult to navigate. One useful new website is [ScanMedicine](#), which gives patients, healthcare professionals, and researchers easy access to information about clinical trials and medical devices brought together from over 11 databases.
- **Join a national register:** Increasingly, there are registers that – with permission – use coded information in the various health data records to find and contact people who are eligible to take part in clinical trials. Such registers include the [National Institute for Health and Care Research BioResource](#) and the [Scottish Health Research Register & Biobank](#). In some cases, the register gives people the power to self-refer for clinical trials where it is safe and appropriate. Other similar digital recruitment services are being set up across the UK and/or linked to pre-existing services.
- **Contact a rare condition support organisation:** Many rare conditions have groups or charities run by and for people living with a

² The Academy is not responsible for content of third-party websites.

particular rare condition and their families. (The umbrella organisation for all rare conditions is **Rare Diseases UK** for the UK and **EURORDIS** for Europe.) These organisations can often help people living with rare conditions find out about clinical trials.

- **Join a patient registry:** A patient registry is usually run by an organisation that collects data over time about a group of people living with a particular condition, with their permission. They are sometimes used to find people to take part in relevant clinical trials. The data in these registries can also become part of the evidence base considered in a clinical trial, reducing the number of people needed to participate. Some kinds of clinical trials – registry-based studies – can be carried out using only data collected in a patient registry, reducing the time and money needed to complete the trial. You can ask the relevant rare disease support organisation or your clinician if you want to find out whether there is a patient registry you can join.